**Clothianidin Executive Summary for Biological Evaluation**

A biological evaluation (BE) is a generic term for an analysis that a federal agency conducts when it takes action subject to review under the Endangered Species Act (ESA). EPA prepares a BE to evaluate the potential effects of an agency action (here registered uses of clothianidin (PC Codes: 044309) on listed and proposed species and designated and proposed critical habitat). This BE encompasses the review of all the registered uses, and the approved product labels for all pesticide products containing clothianidin.

Under its current approach for registration review for conventional pesticides, EPA meets its ESA obligations through a three-step process. EPA’s development of this BE includes two steps. In Step 1, for each listed species and each designated critical habitat, EPA evaluates whether the registered uses of clothianidin will have No Effect (NE) or if the registered uses May Affect (MA) an individual of such species or habitat (separate determinations made for each species and critical habitat). More specifically, Step 1 is intended to be a conservative screen that is heavily reliant upon overlap of (1) areas where an environmentally discernable effect could occur from any labeled use of the pesticide being assessed (assumes the pesticide could be used in all areas allowable on the label) with (2) areas where species range/designated critical habitat occurs. It uses conservative assumptions and is intended to screen out species that are not reasonably expected to be exposed to the pesticide because they are outside of the pesticide use area. If EPA determines there is no effect, that is the end of the analysis for that particular species.

In Step 2, for those species and critical habitats that EPA determines an individual may be affected, EPA uses additional information to determine if clothianidin may affect but is Not Likely to Adversely Affect (NLAA) or may affect and is Likely to Adversely Affect (LAA) each individual species or critical habitat. Step 2 uses a more refined spatial overlap with specific pesticide use sites to calculate the portion of the population exposed, considers life history information, considers actual pesticide applications (usage data), additional toxicity data, and a range of potential exposure concentrations. If EPA makes a NLAA determination, then EPA must informally consult with the Services. Otherwise, if EPA makes a LAA determination, EPA must engage in formal consultation with the Services. Details on the method, models and tools used for making NE, NLAA and LAA determinations are provided in the Revised Method document.[[1]](#footnote-2)

Practically, the LAA threshold for a BE is very conservative as the likely “take” of even one individual of a species triggers LAA (even if that species is almost recovered). This often results in a high number of May Affect determinations in a BE. An LAA determination in the BE, however, should not be interpreted to mean that EPA has made a determination that clothianidin is putting a species in jeopardy. Those determinations are made in the course of Step 3 by the National Marine Fisheries Service and the Fish and Wildlife Service (referred to as The Services).

Step 3 is part of the formal consultation process. Here, the Services prepare a biological opinion (BiOp), which builds upon EPA’s BE to determine whether the potential adverse effect will jeopardize the continued existence of a species or destroy or adversely modify critical habitat. The analysis in Step 3 considers whether the anticipated adverse effects to individuals described in the BE will negatively affect populations and the species they comprise such that they jeopardize the continued existence of the species.

# General Information

Clothianidin is in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with clothianidin, thiamethoxam, and dinotefuran. The mode of action for neonics on target insects (terrestrial and aquatic) involves out-competing the neurotransmitter acetylcholine for available binding sites on the nAChRs proteins (Zhang *et al*. 2008)[[2]](#footnote-3). At low concentrations, neonicotinoids cause excessive nervous stimulation and at higher concentrations, insect paralysis and death will occur (Tomizawa and Casida 2005[[3]](#footnote-4)). In plants, clothianidin is mobile in the xylem and phloem and is readily taken up by the roots and translocated throughout the plant via the transpiration stream. As such, clothianidin kills feeding insects via ingestion or direct contact routes of exposure. Clothianidin is used on a wide variety of agricultural crops. Non-agricultural uses include applications to turf, poultry houses, and ornamentals.

This BE assesses all uses on all currently registered labels. Maximum application rates and minimum application retreatment intervals are based on the use defined by the Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review[[4]](#footnote-5) and addendum[[5]](#footnote-6), unless otherwise noted. **APPENDIX 1-2** provides the use information as further refined by EPA, summarizing details relevant for modeling the maximum use patterns. **APPENDICES 1-2** and **3-1** provide additional details on how these uses were modeled.

There are currently 46 registered Section 3 end-use products for clothianidin. Registered uses include a wide array of agricultural crops, including but not limited to: root and tuber vegetables, leafy vegetables, brassica, cucurbits, fruiting vegetables, cereal grains, citrus fruit, pome fruit, stone fruit, berries, tree nuts, beans and other legumes, herbs, cotton, and tobacco. Clothianidin is also registered for several non-agricultural uses, including commercial premises, outdoor residential, ornamentals trees, turf, and livestock areas. Applications may be made via a variety of methods including aerial and ground foliar sprays, soil treatment (*e.g.*, drench), chemigation (*e.g.*, soil incorporation or foliar), granular, seed treatment, and outdoor bait placement. Maximum single foliar application rates for clothianidin range from 0.05-0.2 lb a.i./A for agricultural uses. Maximum single application rates of 0.4 lb a.i./A are associated with the non-agricultural uses.

Nationally, among surveyed agricultural crops, clothianidin usage has shown an overall increasing trend in pounds applied and total acres treated since 2005 with a slight decrease in 2018. During the most recent five years of available survey data (2014 -2018), less than 50,000 pounds of clothianidin were applied to less than 500,000 acres of agricultural crops annually, in 25 states. During this time frame, the crops with the most usage in terms of annual average total pounds of active ingredient applied were cotton (8,000 lbs), potatoes (5,000 lbs), and soybeans (5,000 lbs). The crops with the most usage in terms of total treated acreage were the same with 100,000, 90,000 and 40,000 acres treated for soybeans, cotton, and potatoes, respectively (see **APPENDIX 1-4** for details). Approximately 50% of clothianidin’s agricultural applications are comprised of four crops (cotton, potatoes, soybeans and broccoli). In terms of total acres treated, approximately 50% of the acres treated with clothianidin are planted with two crops (cotton and soybeans). The remaining clothianidin applications are spread over 20 other crops (e.g., leafy vegetables, cucurbits, fruiting vegetables, cereal grains, citrus fruit, pome fruit, stone fruit, berries, tree nuts, and beans and other legumes). While the vast majority of clothianidin is only applied to a handful of crops, examination of the percent of individual crops grown by state that are treated with clothianidin indicates that usage is prevalent for certain crops in certain states. For instance, an average of 55% of peaches in South Carolina, 75% and 65% of apples in Virginia and West Virginia respectively and 75% of pumpkins in Texas are treated annually with clothianidin **(APPENDIX 1-4)**.

Over 9,000 pounds of clothianidin are applied to non-agricultural sites annually. Most recent non-agricultural usage data from 2013 or 2016 depending on the use site (see **APPENDIX 1-4** for details) show that the largest uses in terms of average annual pounds applied are broad spectrum treatment and bed bug treatment**.** Other use sites are either not surveyed at the national level or no usage was reported.

Seed treatment with clothianidin is generally considered to be widespread in terms of the number of crops and the percentage of the crop planted with treated seed. However, quantitative seed treatment usage data are difficult to obtain due to the complexities of capturing this usage information from growers. While verifiable quantitative usage data that indicate the total pounds of active ingredient used to treat seed or the location and the number of acres planted with treated seed are not currently available, applications of clothianidin to seed and seed pieces may be generally characterized as commonly used on a wide variety of crop seeds and seed pieces for planting based on extension recommendations and other information.

The major transport routes of clothianidin off the treated area include runoff and spray drift for broadcast uses. Clothianidin has a high solubility, low octanol-water partitioning coefficient, low vapor pressure, and low Henry’s Constant. These data suggest that clothianidin has a low potential for volatilization and bioaccumulation. The major route of dissipation for clothianidin appears to be photolysis, with an aqueous photolysis half-life less than 1 day and a soil photolysis half-life of 34 days. The preponderance of clothianidin surface water detections are in agricultural areas and in the vicinity of local use areas. Additional details on the fate of clothianidin are provided in **Chapter 3** of the BE.

# Toxicity Summary

Clothianidin is practically non-toxic to fish on an acute toxicity basis and effects growth following chronic exposure. For aquatic invertebrates, the level of sensitivity to clothianidin varies greatly among species on an acute toxicity basis. For example, clothianidin is practically non-toxic to water fleas (*Daphnia magna*) but is very highly toxic to other taxa such as aquatic insects. Reproduction is affected in both freshwater and estuarine/marine invertebrates. Effects on development are also observed in benthic invertebrates. Effects on yield are observed in both aquatic vascular and non-vascular plants, but only at relatively high-test concentrations (compared to aquatic invertebrates). In terrestrial organisms, clothianidin is characterized as moderately toxic to birds on an acute oral exposure basis and practically nontoxic on a subacute dietary exposure basis. Effects on eggshell thinning represent the most sensitive chronic toxicity endpoint, which is observed in the Northern bobwhite quail. Clothianidin is classified as moderately toxic to mammals on an acute oral exposure basis. Chronic exposure with the Norway rat (*Rattus norvegicus*) results in effects on growth and maturation in offspring. Clothianidin is also highly toxic to bees on an acute basis, and available data suggest potential effects to honeybee and bumble bee colonies, that manifest as decreases in brood and number of adults. Clothianidin exhibits low toxicity to terrestrial plants. From 2010 to 2018, there were 49 ecological incidents categorized as possible to highly probable in their certainty that clothianidin was involved in the incident. There are 4 additional backlogged incidents (i.e., those that have not been fully investigated, and do not have a certainty classification) from 2017-2020 but appear to be related to clothianidin usage. Ecological incidents involving clothianidin have been reported for all assessed taxa except reptiles, amphibians, aquatic invertebrates, and aquatic plants.

Available toxicity data for aquatic taxa indicate that, in general, the degradates of clothianidin are of similar toxicity (non-toxic) or less toxic than parent clothianidin. However, TMG is of concern to benthic invertebrates based on reductions in larval emergence. Because the mobility of clothianidin and its degradates indicate that they do not readily bind to soil or sediment, unextracted residues were not considered for further analysis. Therefore, the stressors of concern for the aquatic assessment are determined to be clothianidin as well as the degradate TMG. For the terrestrial assessment, the stressor of concern is clothianidin only. Consideration of the potential increased toxicity of formulations is considered through the selection of toxicity endpoints and is discussed further in **Chapter 2**.

# Exposure Methods

Exposure estimates are based primarily on fate and transport model results. Aquatic exposures (surface water and benthic sediment pore water) are quantitatively estimated for representative clothianidin uses in specific geographic regions within generic habitats (referred to as bins) using the Pesticide Root Zone Model (PRZM5) and the Variable Volume Water Model (VVWM)[[6]](#footnote-7) in the Pesticides in Water Calculator (PWC). Aquatic exposure results for the bin(s) most appropriate for the species and/or critical habitat are discussed in **Chapter 3**. Also discussed in **Chapter 3** are available water monitoring data for clothianidin. For terrestrial exposures, existing models [*i.e.*, AgDRIFT, earthworm fugacity model, Terrestrial Herpetofaunal Exposure Residue Program Simulation (T-HERPS), Terrestrial Residue Exposure model (T-REX) and portions of the Terrestrial Investigation Model (TIM)] were combined and modified into a single tool that is referred to as the MAGTool (**Chapter 4**). This assessment replaces EPA’s TerrPlant model with the Plant Assessment Tool (PAT). The latter is a more refined exposure model for terrestrial, wetland and aquatic plants.

# Overlap Analyses

Step 1 of the BE involves an analysis of the potential overlap of the action area and individual species ranges and critical habitat. The action area was derived in ArcGIS 10.8 by combining the data layers representative of clothianidin uses and then buffering them out to the off-site transport distance estimated using the AgDRIFT model (**APPENDIX 1-6**). The overlaps of action area and individual species’ ranges or critical habitats were calculated. This analysis used spatial data of species’ ranges and critical habitats from the FWS and NMFS. In the contiguous United States (ConUS), agricultural potential use sites are represented using the USDA Crop Data Layer (CDL) (**APPENDIX 1-5**). All species or critical habitats with some overlap of the action area and their range or designated critical habitat, or with some overlap on species that the listed species depends on (**Chapter 4**) move on to step 2 and are assessed to make LAA/NLAA determinations.

# Effects Determinations

This BE makes effects determinations (NE, MA, NLAA, or LAA)[[7]](#footnote-8) for 1821 listed species, and 791 designated critical habitats. Under Step 1, EPA made NE determinations for 259 species and 131 critical habitats because there was not overlap between the species range/critical habitat and the action area. EPA made MA determinations for 1562 species and 660 critical habitats. As explained above, all species and critical habitats with a MA determination progressed to the Step 2 analysis where an NLAA or LAA determination is made[[8]](#footnote-9). In Step 2, EPA made NLAA determinations for 337 species and 214 critical habitats. EPA made LAA determinations for 1225 species and 446 critical habitats. Specific species determinations are provided in **APPENDIX 4-1.**

For each LAA determination, EPA also grouped these determinations into three categories (*i.e.,* strongest, moderate and weakest) which characterize the strength of the weight of evidence. Each species or critical habitat was assigned a weak, moderate or strong evidence in the LAA determination based on multiple factors, including: the impact of using less conservative assumptions in the analysis, the quality of the species range or usage data, whether impacts could occur due to direct toxicity to the species or to both direct toxicity and to its prey, pollination, habitat, and dispersal (PPHD), the presence of reported incidents involving the species taxa or PPHD taxa, the presence of monitoring data that exceeds endpoints, whether species’ habitats are potential use sites or if they could only be exposed from spray drift, and the likelihood of drift into a species habitat (*e.g*., if the species inhabits forests).

Of the LAA determinations, the majority (81% of species and 78% of critical habitats) were considered to have moderate evidence. Strongest evidence was found for none of the species or critical habitat LAA determinations. Weakest evidence was found for 19% of species and 22% of critical habitat LAA determinations. Open Space Developed, Developed, and Poultry Litter (considered a non-agricultural use as it relates to the application of manure contaminated with clothianidin rather than a direct application of clothianidin) were the use sites most frequently associated with predicted impacts to species or critical habitats with LAA determinations. LAA determinations were made for species across all taxa. Because clothianidin is highly toxic to terrestrial and aquatic invertebrates but is much less toxic to other vertebrate and plant taxa, 1225 of the 1057 LAA determinations were based on effects to PPHD alone (see **Table 4-7** in **Chapter 4**). Having impacts only to PPHD also contributes to the high number of moderate strength of evidence classifications.For certain species, there were uncertainties in the clothianidin effects determinations based on the resolution of spatial data. For species and critical habitats, there were uncertainties in the resolution of usage data and the threshold for assessing impacts on PPHD (detailed in **Chapter 4**).**Table 1** and **Table 2** summarize the NE, NLAA and LAA determinations for species and critical habitats. **Table 3** summarizes the strength of evidence classifications for the LAA determinations.

EPA makes an LAA determination when there is the potential for a single individual of a species to be affected by the labeled use of a pesticide, which is a conservative threshold. This often results in a high number of LAA determinations. An LAA determination in the BE should not be interpreted to mean that EPA has determined that the registered use of imidacloprid is putting a listed species in jeopardy. The National Marine Fisheries Service and the Fish and Wildlife Service make those determinations.

**Table 1. Summary of Species Effects Determinations for Clothianidin (Counts by Taxon).**

|  |  |  |  |
| --- | --- | --- | --- |
| **Taxon** | **Step 1 Effects Determinations** | **Step 2 Effects Determinations** | **Totals** |
| **No Effect** | **May Affect** | **Not Likely to Adversely Affect** | **Likely to Adversely Affect** |
| Mammals | 1 | 101 | 46 | 55 | 102 |
| Birds | 6 | 102 | 31 | 71 | 108 |
| Amphibians | 0 | 39 | 0 | 39 | 39 |
| Reptiles | 8 | 39 | 13 | 26 | 47 |
| Fish | 4 | 187 | 13 | 174 | 191 |
| Plants | 72 | 878 | 175 | 703 | 950 |
| Aquatic Invertebrates | 151 | 72 | 34 | 38 | 223 |
| Terrestrial Invertebrates | 17 | 144 | 25 | 119 | 161 |
| **Total** | **259** | **1562** | **337** | **1225** | **1821** |
| **Percent of total** | **14%** | **86%** | **19%** | **67%** |  |

**Table 2. Summary of Critical Habitat Effects Determinations for Clothianidin (Counts by Taxon).**

|  |  |  |  |
| --- | --- | --- | --- |
| **Taxon** | **Step 1 Effects Determinations** | **Step 2 Effects Determinations** | **Totals** |
| **No Effect** | **May Affect** | **Not Likely to Adversely Affect** | **Likely to Adversely Affect** |
| Mammals | 0 | 33 | 17 | 16 | 33 |
| Birds | 2 | 29 | 3 | 26 | 31 |
| Amphibians | 0 | 26 | 0 | 26 | 26 |
| Reptiles | 5 | 11 | 5 | 6 | 16 |
| Fish | 3 | 102 | 5 | 97 | 105 |
| Plants | 64 | 396 | 165 | 231 | 460 |
| Aquatic Invertebrates | 50 | 21 | 3 | 18 | 71 |
| Terrestrial Invertebrates | 7 | 42 | 16 | 26 | 49 |
| **Total** | **131** | **660** | **214** | **446** | **791** |
| **Percent of total** | **17%** | **83%** | **27%** | **56%** |  |

**Table 3. Classification of LAA Determinations by Strength of Evidence.**

|  |  |  |
| --- | --- | --- |
| **Strength of LAA call** | **Species range** | **Critical Habitat** |
| **Number** | **% of LAA determinations** | **Number** | **% of LAA determinations** |
| Strongest evidence of LAA | 0 | 0% | 0 | 0% |
| Moderate evidence of LAA | 994 | 81% | 349 | 78% |
| Weakest evidence of LAA | 231 | 19% | 97 | 22% |

1. https://www3.epa.gov/pesticides/nas/revised/revised-method-march2020.pdf [↑](#footnote-ref-2)
2. Zhang, Y, Liu, S, Gu, J, Song,F, Yao, X, Liu, Z. 2008. Clothianidin acts as an antagonist on insect nicotinic acetylcholine receptor containing the Y151M mutation. Neuroscience Letters. 446:97– 100. [↑](#footnote-ref-3)
3. Tomizawa, M, Casida, J. 2005. Neonicotinoid insecticide toxicology: mechanisms of Selective Action.

Annual Review of Pharmacology and Toxicology, 45, 247–268. [↑](#footnote-ref-4)
4. *Clothianidin – Transmittal of the Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessments to*

 *Support Registration Review*. Environmental Protection Agency, Office of Pesticide Programs, Environmental

Fate and Effects Division, November 27, 2017. [↑](#footnote-ref-5)
5. *Clothianidin Non-pollinator Addendum and Chenical-specific Response to Comments for Public Comments Received on the Registration Review Preliminary Pollinator and Preliminary Non-pollinator Risk Assessments.* Environmental Protection Agency, Office of Pesticide Programs, Environmental Fate and Effects Division, January 8, 2020. [↑](#footnote-ref-6)
6. The exposure models can be found at: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment> [↑](#footnote-ref-7)
7. NE = No effect. MA = May affect. NLAA = Not likely to adversely affect. LAA = Likely to adversely affect. [↑](#footnote-ref-8)
8. Available at: <https://www.epa.gov/endangered-species/revised-method-national-level-listed-species-biological-evaluations-conventional> [↑](#footnote-ref-9)